Glasgow contributions to human gene mapping

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The Genetics Department at Glasgow University started with the appointment of Guido Pontecorvo (1907-1999) to a Lectureship in Genetics in 1945 and this was followed by his promotion to a new Chair of Genetics in 1955. Ponte, as he liked to be called, had been a PhD student (1939-41) with Herman Muller in Edinburgh and had moved in 1941 to a research post in the Zoology Department in Glasgow. Ponte's great contribution was his work on tetrad analysis, mitotic crossing-over and haploidisation in *Aspergillus nidulans* that led to his finding of intragenic recombination and the discovery that the gene could be divided into smaller units, later known as cistrons, each recognisable by mutation. This work was reported just prior to the publication of the Watson and Crick model of the DNA double helix. His exploitation of what he termed the parasexual cycle (in distinction to the sexual or meiotic cycle) led Ponte to the notion that, if somatic crossing over could be studied in cultured human cells, the problems of human gene mapping could be overcome; these problems were the impossibility of experimental breeding, the small number of progeny and long generation times. His ideas were encapsulated in a series of lectures presented in 1956 at Columbia University and published in a monograph entitled Trends in Genetic Analysis [1] (Pontecorvo, 1958). Somatic recombination, chromosomal nondisjunction and haploidisation were the essential elements to be harnessed in the construction of a human gene map from cultured cells. Progress in achieving these strategies was hampered by a lack of analysable polymorphic markers and Ponte's approach did not bear fruit by the time he left Glasgow in 1968 to join Michael Stoker at the ICRF. Within two years segregation of human chromosomes in human:mouse somatic cell hybrids had emerged to substantiate Ponte's vision. Interspecies biochemical variants provided an abundance of polymorphisms for chromosomal assignment and gene ordering. Ponte joined in the research on somatic cell hybrids at ICRF and his contributions included the discovery (1975) that polyethylene glycol could be used instead of Sendai virus to induce man:mouse hybrids [2].

I believe that the *first ever* contribution to human gene mapping came from Glasgow in 1937, well before the establishment of the Genetics Department. This came from Professor W J

Brownlow Riddell, Head of the Department of Ophthalmology. One of his interests was colour blindness and, prompted most likely by Julia Bell, he looked for genetic linkage between the X-linked loci for haemophilia and colour vision defects. Three of the fourteen haemophiliac families he tested also segregated for colour blindness and the first revealed the only recombinant included in the famous paper of Bell and Haldane [3](1937) that described the first example of genetic linkage in humans. As Riddell's paper (also1937) [4] on this family was published three months earlier that the Bell and Haldane paper, it can be said that Riddell was the first to report crossing-over in humans. The initial rough estimate of 5% recombination between the two loci was reinvestigated by Haldane and Smith in 1947 [5] in seventeen families (including the three contributed by Riddell) and a new estimate of 9.8% recombination was reported. While the first human linkage involved the X chromosome, the first autosomal linkage was reported by Jan Mohr in 1951 [6], between the Lutheran and Lewis (including Secretor) blood groups. Mohr found a hint that the gene for myotonic dystrophy belonged to the same linkage group and this was confirmed in the paper by Renwick et al, in 1971 [7].

The complex work on somatic recombination in cultured cells was in progress in the Glasgow Genetics Department in 1959 when James H Renwick (1926-1994) joined as Senior Lecturer to continue his work from the Galton Laboratory on human gene mapping by classical genetic linkage analysis, supported by a novel computer programme he was developing with colleagues in Baltimore. With Marian Izatt he set up a marker lab to test common blood groups and other polymorphisms in serum and red cell enzymes that could be used to test for linkage in families with genetic disorders and dominant traits. Renwick felt that a word was needed to indicate that loci separated by 50% recombination could be on the same chromosome and so he coined the useful word "syntenic". Synteny is now a genetic term in common usage. During the 1960s blood samples from such families streamed into the marker lab for testing. Renwick's publications on linkage arising out of his nine years work in Glasgow before moving to UCL in 1968 are listed in Table 1. They include follow-up studies on the famous ABO: Nail-patella syndrome linkage [8] discovered by Renwick and Lawler (1955) and the first gene assignment to a human autosome [9], namely Duffy blood group to HSA1 (Donohue et al 1968). Other notable findings on the list are the assignment of haptoglobin to HSA16 [10] (Robson et al 1969), the linkage between Duffy and zonular cataract [11](Renwick and Lawler, 1963) and confirmation of the linkage between Secretor and myotonic dystrophy [7] (Renwick et al 1971). It should be noted that all these linkages

were with polymorphisms tested by the marker lab. Among disease families that failed to show linkage were several extensive pedigrees of multiple self–healing squamous epithelioma [12] (MSSE or Ferguson-Smith disease, 1934). This condition was mapped later to HSA9q23 (Goudie et al 1994) using DNA markers [13], but it took a further 17 years before mutations were found in TGFBR1 [14] (Goudie et al 2011). Review in 1994 of the 1971 Glasgow linkage analysis revealed a low positive lod score with ABO. A number of other disease gene loci were mapped by genetic linkage analysis in Glasgow, including multipoint mapping of the DMD region in Xp [15] (Wilcox et al, 1985), the gene for hereditary persistence of alphafetoprotein to human chromosome 4q [16] (HSA4q, Ferguson-Smith et al, 1985), the Emery-Dreifuss muscular dystrophy gene to Xq28 [17] (Yates et al, 1986), and the gene for tuberous sclerosis type 1 to HSA9q33 [18](Connor et al, 1987).

In 1961 I returned to Glasgow after three years in Baltimore to take up a Lectureship with Ponte and to work on human chromosomes. From 1956-59 I had worked on sex chromatin with Bernard Lennox at the Glasgow University Pathology Department at the Western Infirmary and our buccal smear surveys had revealed for the first time cases of Klinefelter syndrome in 11% of severe male infertility and 1% of males with learning difficulty. My trip to Baltimore in February 1959 was to improve my attempts to make chromosome preps in these patients and, as a Fellow with Victor McKusick, I trained in medical genetics, ran a chromosome diagnostic laboratory and undertook research on sex chromosome abnormalities with Lawson Wilkins and Howard Jones. We were able to map, by haploidisation, a stature gene and genes controlling the Turner phenotype to the short arm of the X and to homologues on the Y chromosome [19] (Ferguson-Smith, 1965). In other words, Turner syndrome was caused by haploinsufficiency of genes on the X that escaped inactivation in normal women and had active homologues on the Y. This helped to explain the Klinefelter phenotype on the basis of increased dosage of X-Y linked genes. Klinefelter patients with more than two X chromosomes had additional skeletal abnormalities and greater learning difficulties. On returning to Glasgow I revisited and karyotyped our Klinefelter patients and, at the same time, tested their colour vision (and their parents) to determine the origin of nondisjunction; blood was also taken for XG blood group studies in collaboration with Ruth Sanger for the same purpose. Our XG blood group results in Klinefelter patients with a 46,XX karyotype suggested that illegitimate X-Y recombination beyond the pseudoautosomal boundary had resulted in the exchange of the testis-determining locus on the Y for the XG locus on the X

and that these two loci must map just outside the boundary [20](Ferguson-Smith, 1966). This was confirmed much later by FISH mapping [21] (Ferguson-Smith, 1988) and by the positional cloning of the SRY gene [22] (Sinclair et al, 1990).

The chromosome diagnostic service work in Glasgow and our efforts to improve chromosome identification led to the identification of families with chromosome heteromorphisms potentially useful for gene mapping. This was reinforced by the report of the Duffy: HSA1 assignment by Donohue et al [9] (1968). A series of 84 such families were assembled and tested by the marker lab with largely negative results. One family segregating for a centric heteromorphism of HSA16 gave positive lod scores for haptoglobin [23] (Wikramanayake et al, 1971) and this contributed to the haptoglobin assignment made by Robson et al, [10](1969). The remaining negative results were not entirely wasted as they enabled markers to be excluded from many chromosomal regions. The exclusion map was reported by Ferguson-Smith et al [24] (1975) and additional exclusions from chromosomal deletions were added at later HGM Workshops [25, 26] (Aitken et al, 1976, 1978).

Chromosomal deletions and duplications detected by the cytogenetics lab as part of the West of Scotland Regional Genetics Service provided the raw material for deletion mapping by haploidisation of many of the blood group and other polymorphisms investigated by the marker lab which I had continued after Renwick's departure to London in 1968. The first ever human gene to be mapped by deletion mapping was red cell acid phosphatase to the distal end of HSA2p [27] (Ferguson-Smith et al, 1973). Our patient was a child with developmental malformations and learning difficulties whose father was a balanced 2p;5q translocation carrier and who was homozygous for the B allele at the AcP locus. The mother was homozygous for the A allele and the homozygous state of both parents was confirmed by enzyme assay of AcP. The child typed for the A allele and was hemizygous on enzyme assay. It was concluded that the paternal B allele had been lost in the HSA2p23-pter deletion in the child and this interpretation was confirmed subsequently by mapping results of other groups. Additional chromosomal assignments of polymorphic loci followed from our cytogenetics and marker labs and these are listed in Table 2. Most of these were presented at the Human Gene Mapping Workshops from 1973 onwards. For example, a series of unbalanced HSA9 translocations was highly informative in the precise mapping of both adenylate kinase (AK1) and galactose-1-phosphate uridyl transferase (GALT) to 9q34 and 9p13 respectively [28, 29] (Ferguson-Smith et al, 1976; Ferguson-Smith and Aitken, 1982).

As the AK1 locus was closely linked to the ABO:Nail-patella linkage all three loci could be assigned to 9q34. One GALT family was particularly interesting as the mother with a balanced 9:11 translocation was homozygous for the Duarte variant allele and so had an enzyme activity 50% less than normal [29]. Her two offspring with duplications of 9p13 had GALT levels equivalent to normal resulting from the two maternal variant alleles and the single normal paternal allele. In two other interesting families, glutamate oxaloacetate transaminase (GOTs) was assigned to HSA10q24-25 from unbalanced translocations with breakpoints at 10q23 in one family and 10q26 in the other; a GOTs allele was deleted in the former but not in the latter [30] (Aitken and Ferguson-Smith, 1978).

X-chromosome deletions discovered in Glasgow have also been informative for the human gene map. Our large series of Duchenne muscular dystrophy (DMD) families that contributed to the joint project that identified the dystrophin gene [31] (Kunkel et al, 1986) included a DMD patient with short stature and learning difficulties and a 6 megabase Xp deletion by flow cytometry [32](Wilcox et al, 1986). In a similar case reported by Franke et al (1985), and cited in [32], the DMD locus was deleted together with loci for retinitis pigmentosa, chronic granulomatous disease and the McLeod syndrome. This deletion was also measured in Glasgow at approximately 6Mb. None of these disorders were found in the Glasgow patient, probably indicating that this linkage group must extend over more than 6Mb. In another Glasgow family a male child born with ichthyosis due to steroid sulphatase (STS) deficiency proved to have a Xp22.3-pter deletion due to a maternal Xp23:Yq13 translocation [33]; he had a normal Y chromosome. The mother was short in stature but had no other features of Turner syndrome. The child's maternal grandparents had normal sex chromosomes and it seems that the X:Y rearrangement must have occurred at meiosis in the grandfather. This individual had an Xga+ve allele at the XG locus but had failed to pass this to the child's mother who, like her mother was Xg-ve. This maps the XG and STS loci to within the Xp23-pter deletion in the mother and child [33] (Ferguson-Smith et al, 1982). The conclusion is confirmed by STS assay which shows no STS activity in the child and half the expected activity in the mother. The result is of special interest to the Glasgow lab as it supports our 1966 prediction from XX males that the XG locus maps to Xp just outside the pseudoautosomal boundary [20]. Further confirmation came the following year from studies that revealed that 12E7, a gene associated with XG, maps close to the XY pairing segments [34] (Goodfellow et al, 1983).

The interest of the Glasgow cytogenetics lab in human sex chromosomes led to a long term project to make a physical map of the Y chromosome. As crossing-over occurs only in the small pairing segments, the map could not be made in the much larger differential segment by genetic linkage analysis and so recourse had to be made to deletion mapping. Recombinant clones containing single copy Y sequences were isolated from several Y chromosome–specific libraries made from interspecific cell hybrids. These were mapped by Southern blotting to genomic DNA from patients with known Y chromosome aberrations, mostly deletions detected during infertility investigations, or from XX males in which X-Y interchange had transferred variable lengths of Yp to the X [35, 36] (Affara et al, 1986, Ferguson-Smith et al, 1987). The order of 39 Yp probes was determined in 25 XX males that separated the Y short arm into 17 intervals. A similar map for the Y long arm was constructed with 37 DNA probes that ordered them into 14 separate intervals. Exceptions to the consensus order occurred in 23% of Yp aberrations and 12% of Yq aberrations due mostly to inversions. The resulting map has been useful in determining breakpoints in patients with presumptive Y aberrations.

In 1969 Pardue and Gall [37] made the first *in situ* hybridisations (ISH) when they mapped radiolabelled repetitive mouse satellite DNA to the paracentric regions of mouse chromosomes. An attempt to map the globin genes using labelled messenger RNA from rabbit reticulocytes in 1972 failed because the mRNA could not be made sufficiently radioactive to give a specific signal on human chromosomes. With the advent of recombinant DNA technology, a joint Glasgow project with Bob Williamson from the Beatson Institute, and funded by the MRC, revisited the possibility of mapping single copy genes by ISH. We developed the method using tritiated thymidine labelled ribosomal RNA from Xenopus laevis, cloned in a plasmid vector and detected on metaphase acrocentric chromosomes by autoradiography using liquid photographic emulsion [38] (Malcolm et al, 1977). This success was followed by making cRNA probes from cloned genomic DNA of both ² - and ±- globin genes which hybridised successfully to the short arms of HAS11 and HAS16 respectively [39, 40, 41] (Malcolm et al,1881; Barg et al 1981, 1982). These proved to be the first regional assignments of single genes by ISH. We then mapped the kappa light chain immunoglobulin gene locus to HSA2p later the same year [42] (Malcolm et al, 1982). Among the many applications of ISH, the mapping of cloned Y chromosome probes to the end of the short arm of one of the two Xs in XX males was particularly satisfying [21]

(Ferguson-Smith 1988). Radioactive labelling of probes was soon replaced by fluorescence labelling and FISH then became the most widely used method for gene assignment.

In 1987 several of those involved in human gene mapping in Glasgow moved to appointments at the Cambridge University Department of Pathology and worked on a programme entitled the Molecular Pathology of Disease funded by the MRC. Research continued on human gene mapping, positional cloning of disease genes and comparative genomics. Contributions from Glasgow and Cambridge after this date are recorded elsewhere.

It may be of interest to note that many of the cytogenetic approaches described in this article depend on nondisjunction and haploidisation, two of the three elements advocated by Pontecorvo sixty years ago as likely to be the most productive in the construction of a human gene map. Glasgow can be proud of its contributions to this endeavour.

References

1. Pontecorvo G (1958) *Trends in Genetics.* Columbia Biological Series, Columbia University Press, New York.

2. Pontecorvo G (1975) Production of mammalian somatic cell hybrids by means of polyethylene glycol treatment. *Somatic Cell Genetics* 1:397-400.

3. Bell J, Haldane JBS (1937) The linkage between colour blindness and haemophilia in man. *Proc Roy Soc B* 123:119-150.

4. Riddell WJB (1937). Haemophilia and colour blindness occurring in the same family. *Brit J Ophthalmol* 21:113-116.

5. Haldane JBS, Smith CAB (1947) A new estimate of the linkage between the genes for colour blindness and haemophilia in man. *Ann Eugenics* 13:10-31

6. Mohr J (1951) Estimation of linkage between the Lutheran and the Lewis blood groups. *Acta Path Microbiol Scand* 29:339-344.

7. Renwick JH, Bundey S, Ferguson-Smith MA, Izatt MM (1971) Confirmation of linkage of the loci for myotonic dystrophy and ABH secretion. *J. Med. Genetics* 8: 407-416.

8. Renwick JH, Lawler SD (1955) Genetical linkage between the *ABO* and nail-patella loci. *Ann Hum Genet* 19:312-331.

9. Donahue RP, Bias WB, Renwick JH, McKusick VA.(1968) Probable assignment of the Duffy blood group locus to chromosome 1 in man. *Proc Nat Acad Sci USA* 61:949-955.

10. Robson B, Polani PE, Dart SJ, Jacobs PA, Renwick JH.(1969) Probable assignment of the alpha locus of haptoglobin to chromosome 16 in man. *Nature* 223:1163-1165.

11. Renwick JH, Lawler SD. (1963) Probable linkage between a congenital cataract locus and the Duffy blood group locus. *Ann Hum Genet* 27:67-84.

12. Ferguson-Smith J. (1934) A case of multiple primary squamous-celled carcinomata of the skin in a young man, with spontaneous healing. *Brit J Derm Syph* 46: 267-272.

13. Goudie DR, Yuille MAR, Leversha MA, Furlong RA, Carter NP, Lush MJ, Affara NA,Ferguson-Smith MA. (1993) Multiple self-healing squamous epithelioma (ESSI) mapped to 9q22-q31 in families with common ancestry. *Nature Genetics* 3: 165-169.

14. Goudie DR, D'Allessandro M, Merriman B, Lee H, Szeverenyi I, Avery S, O'Connor BD, Nelson SF, Coats ST, Stewart A, Christie L, Pichert G, Friedel J, Hates I, Burrows N, Whittaker S, Gerdes A, Broesby-Olsen S, Ferguson-Smith MA, Verma C, Lunny DF, Reversade B, Lane EB. (2011) Multiple self-healing squamous epithelioma is caused by a disease-specific spectrum of mutations in *TGFBR1*. *Nature Genetics* 47:365-369.

15. Wilcox DE, Affara NA, Yates JRW, Ferguson-Smith MA, Pearson PL.(1985) Multipoint linkage analysis of the short arm of the human X chromosome in families with X-linked muscular dystrophy. *Human Genetics* 70: 365-375.

16. Ferguson-Smith MA, Yates JRW, Kelly D, Aitken DA, May HM, Krumlauf R, Tilghman SM. (1985) Hereditary persistence of alphafetoprotein maps to the long arm of chromosome 4 . *Cytogenet Cell Genet* 40: 628.

17. Yates JRW, Affara NA, Jamieson DM, Ferguson-Smith MA, Hausmanova-Petrusewicz I, Zaremba J, Borkowska J, Johnston AW, Kelly K. (1986) Emery-Dreifuss muscular dystrophy: localisation to Xq27.3-qter confirmed by linkage to the factor VIII gene. *J. Med Genet* 23: 587-590.

18. Connor JM, Pirrit LA, Yates JR, Fryer AE, Ferguson-Smith MA. (1987) Linkage of the tuberous sclerosis locus to a DNA polymorphism detected by v-abl. *J Med Genet* 24:544-546.

19. Ferguson-Smith MA.(1965) Karyotype-phenotype correlations in gonadal dysgenesis and their bearing on the pathogenesis of malformations. *J Med Genet* 2: 142-155.

20. Ferguson-Smith MA.(1966) X-Y chromosomal interchange in the aetiology of true hermaphroditism and of XX Klinefelter's syndrome. *Lancet* ii: 475-476.

21. Ferguson-Smith MA. (1988) Progress in the molecular cytogenetics of man. *Phil.Trans.R.Soc.Lond. B* 319:239-248.

22. Sinclair AH, Berta P, Palmer MS, Hawkins JR, Griffiths BL, Smith MJ, Foster JW, Frischauf A-M, Lovell-Badge R, Goodfellow PN. (1990) A gene from the human sex determining region encodes a protein with homology to a conserved DNA-binding motif. *Nature* 346: 240–244.

23. Wikramanayake E, Renwick J H, Ferguson-Smith MA. (1971) Chromosomal heteromorphisms in the assignment of loci to particular autosomes: a study of four pedigrees. *Annales de Génétique* 14: 245-256.

24. Ferguson-Smith MA, Ellis PM, Mutchinick O, Glen KP, Coté GB, Edwards JH.(1975) Centromeric Linkage. Rotterdam Conference (1974), Second International Workshop on Human Gene Mapping. *Birth Defects: Original Article Series* XI, 3: 130-137.

25. Aitken DA, Ferguson-Smith MA, Dick HM (1976) Gene mapping by exclusion: the current status. Baltimore Conference (1975): Third International Workshop on Human Gene Mapping. Birth Defects: Original Article Series, XII, 7, 1976. The National Foundation, New York, pp. 256-265.

26. Aitken DA, Ferguson-Smith MA. (1978) The exclusion map up-dated. *Cytogenet Cell Genet* 22: 613-617.

27. Ferguson-Smith MA, Newman BF, Ellis PM, Thomson DMG, Riley I D. (1973) Assignment by deletion of human red cell acid phosphatase gene locus to the short arm of chromosome 2 . *Nature New Biology* 243: 271-274.

28. Ferguson-Smith, M.A., Aitken DA, Turleau C, de Grouchy J. (1976). Localisation of the human ABO;Np-1:AK-1 linkage group by regional assignment of AK-1 to 9q34. *Human Genetics* 34: 35-43.

29. Ferguson-Smith MA, Aitken DA.(1982) The contribution of chromosome aberrations to the precision of human gene mapping. *Cytogenet Cell Genet* 32: 24-42.

30. Aitken DA, Ferguson-Smith M.A. (1978) Gene dosage evidence for the regional assignment of the GOTS structural gene locus to 10q24-10q25. *Cytogenet Cell Genet* 22: 468-471.

31. Kunkel LM and co-authors (1986) Analysis of deletions in DNA from patients with Becker and Duchenne muscular dystrophy. *Nature* 322, 73-77.

32. Wilcox DE, Cooke A, Colgan J, Boyd E, Aitken DA, Sinclair L, Glasgow L, Stephenson JB, Ferguson-Smith MA.(1986) Duchenne muscular dystrophy due to familial Xp21 deletion detectable by DNA analysis and flow cytometry. *Human Genetics* 73, 175-180.

33. Ferguson-Smith MA, Sanger R, Tippett P, Aitken DA, Boyd E. (1982) A familial t(X;Y) translocation which assigns the Xg blood group locus to the region Xp23-pter. *Cytogenet Cell Genet* 32: 273-274.

34. Goodfellow P, Banting G, Sheer D, Ropers HH, Caine A, Ferguson-Smith MA, Povey S, Vos R. (1983) Genetic evidence that a Y-linked gene in man is homologous to a gene on the X chromosome. *Nature* 302: 346-349.

35. Affara NA, Florentin L, Morrison N, Kwok K, Mitchell M, Cooke A, Jamieson D, Glasgow L, Meredith L, Boyd E, Ferguson-Smith MA (1986) Regional assignment of Y-linked DNA probes by deletion mapping and their homology with X-chromosome and autosomal sequences. *Nucleic Acids Research* 14: 5353-5373.

36. Ferguson-Smith MA, Affara NA, Magenis RE. (1987) Ordering of Y-specific sequences by deletion mapping and analysis of X-Y interchange males and females. *Development* 101 Suppl:41-50.

37. Pardue ML, Gall JG.(1970) Chromosomal localisation of mouse satellite DNA. *Science* 168:1356-1358.

38. Malcolm S, Williamson R, Boyd E, Ferguson-Smith MA.(1977) A comparison of in situ hybridisation techniques for gene localisation. *Cytogenet Cell Genet* 19: 256-261.

39. Malcolm S, Barton P, Murphy CST, Ferguson-Smith MA. (1981) Chromosomal localisation of a single copy gene by *in situ* hybridisation: human beta-globin genes on the short arm of chromosome 11. *Ann Hum Genet* 45: 135-141.

40. Barg R., Barton P, Ferguson-Smith MA, Malcolm S. (1981) Chromosomal mapping of human globin genes. *Trans. Biochem. Soc*. 9: 124.

41. Barg R, Barton P, Caine A, Clements RL, Ferguson-Smith MA, Malcolm S., Morrison N, Murphy CS.(1982) Regional localisation of human alpha-globin genes to the short arm of chromosome 16 (16p12-pter) using both somatic cell hybrids and in situ hybridisation. *Cytogenet Cell Genet* 32: 252-253.

42. Malcolm S, Barton P, Murphy C, Ferguson-Smith MA, Bentley DL.(1982) Localization of human immunoglobulin kappa light chain variable region genes to the short arm of chromosome 2 by *in situ* hybridization. *Proc Natl Acad Sci USA* **79**: 4957-4961.

Table 1 J H Renwick: Glasgow papers on human gene mapping by genetic linkage

1962	Elliptocytosis and Rhesus	Bannerman and Renwick	Ann Hum Genet
1963	Duffy and cataract	Renwick and Lawler	Ann Hum Genet
1964	XG and colour blindness	Renwick and Schultz	Amer J Hum Genet
1965	Intraepithelial dyskeratosis	Pollizer et al	Amer J Hum Genet
1965	Nail-patella: parameters	Renwick and Izatt	Ann Hum Genet
1965	Nail-patella: recombination	Renwick and Schultz	Ann Hum Genet
1966	Blood groups	Umansky et al	Vox Sanguinis
1967	Linkage data: storage	Renwick and Bolling	Amer J Hum Genet
1968	Retinal degeneration	Pearce et al	Ann Hum Genet
1968	Duffy blood group: chr 1	Donahue et al	Proc Nat Acad Sci
1969	Haptoglobin: chr 16	Robson et al	Nature
1969	White sponge naevus	Browne et al	Ann Hum Genet
1969	Angiokeratoma: XG	Johnston et al	Ann Hum Genet
1971	Myotonic dystrophy: secretor	Renwick et al	J Med Genet
1971	Chromosome heteromorphisms	Wikramanyake et al	Ann Génétique
1971	Chromosome variations	Renwick	Ann Hum Genet
1971	Multiple self-healing epithelioma	Ferguson-Smith et al	Birth Defects Ser

Table 2. Glasgow chromosomal assignments by deletion/duplication mapping

Acid phosphatase	AcP	2p23-pter	*Nature New Biology* 1973, 243:271-274
Adenylate kinase 1	AK1	9q34	*Human Genetics* 1976, 34:35-43
Glutamic-oxaloacetic transaminase	GOTs	10q24-25	*Cytogenet Cell Genet* 1978, 22:468-471
Nucleoside phosphorylase	NP	14q12-qter	*Cytogenet Cell Genet* 1978, 22:490-492
Haptoglobin alpha	Hp±	16cen-16q22	*Cytogenet Cell Genet* 1978, 22:513
Adenosine deaminase	ADA	20p11-qter	*Cytogenet Cell Genet* 1978, 22:514-517
5S ribosomal RNA	5S	1q42-44	*J Med Genetics* 1979, 16:246-253
Galactose-1-phosphate uridyl transferase	GALT	9p13-cen	*Cytogenet Cell Genet* 1982, 32:24-42
XG blood group	XG	Xp23-pter	*Cytogenet Cell Genet* 1982, 32:273-274
HY antigen	HY	Ycen-qter	*Development* 1987, 101 Supl:157-161